

Prenatal findings and pregnancy outcome in fetuses with right and double aortic arch. A 10-year experience at a tertiary center

ANA-MARIA PETRESCU¹, DAN RUICAN¹, CIPRIAN LAURENȚIU PĂTRU^{1,2}, GEORGE LUCIAN ZORILĂ^{1,2}, ȘTEFANIA TUDORACHE^{1,2}, ALEXANDRU CRISTIAN COMĂNESCU^{1,2}, ANCA-MARIA ISTRATE-OFIȚERU^{1,3,4}, ANNE MARIE BADIU⁵, MIHAI IOANA⁶, GEORGE ALIN STOICA⁷, DOMINIC GABRIEL ILIESCU^{1,2}

¹Department of Obstetrics and Gynecology, Emergency County Hospital, Craiova, Romania

²Department of Mother and Child, University of Medicine and Pharmacy of Craiova, Romania

³Department of Histology, University of Medicine and Pharmacy of Craiova, Romania

⁴Research Center for Microscopic Morphology and Immunology, University of Medicine and Pharmacy of Craiova, Romania

⁵Department of Pathology, Emergency County Hospital, Craiova, Romania

⁶Department of Medical Genetics, University of Medicine and Pharmacy of Craiova, Romania

⁷Department of Pediatric Surgery, Emergency County Hospital, Craiova, Romania

Abstract

Objective: Our objective was to evaluate the accuracy of the prenatal diagnosis and the relation between the type of right aortic arch (RAA) with other intra- or extracardiac (EC) and chromosomal anomalies. **Methods:** A retrospective, observational study was conducted between 2011–2020 in a Romanian tertiary center. All RAA cases, including double aortic arch (DAA), were extracted from the databases and studied thoroughly. **Results:** We detected 18 RAA cases: five (27.78%) type I (mirror image, “V” type), 11 (61.12%) type II (“U” type), and two (11.10%) DAA cases. Heart anomalies were associated in 38.89% (overall), 60% (type I), 36.37% (type II), and 0% (DAA) cases. Tetralogy of Fallot represented the most prevalent cardiac malformation (in 22.23% of cases). EC anomalies were present in 44.44% of fetuses (20% of type I, 54.55% of type II, and 50% of DAA cases). Genetic abnormalities were found in 41.17% of pregnancies, with 22q11.2 deletion in 23.53%. 55.55% of the cases had a good neonatal evolution and 44.45% of the pregnancies were terminated. An overall good outcome of pregnancy was noted in 40% of type I RAA, 63.64% of type II RAA, and 50% of DAA cases. All RAA cases examined in the first trimester were correctly diagnosed. **Conclusions:** RAA can be accurately diagnosed and classified by means of prenatal ultrasound since early pregnancy. A detailed anatomy scan and genetic testing, including 22q11 deletion, should be offered to all pregnancies when RAA is discovered. When isolated, RAA associates a good outcome, indifferently the anatomical type.

Keywords: right aortic arch, double aortic arch, congenital heart disease, fetopathology, 22q11 deletion.

Introduction

Right aortic arch (RAA) represents a congenital cardiovascular malformation caused by a disruption in the embryonic development around the 21st day of the intrauterine life, when the formation of the endocardial tube begins [1]. This malformation is characterized by an abnormal laterality of the aorta and therefore of the origin of the brachiocephalic arteries. Thus, these vessels will lie to the right of the trachea [2], leading sometimes to tracheoesophageal compression [3]. The antenatal diagnosis of RAA is important, not only because of this possible respiratory or digestive complications, but also because it should trigger an alarm, due to the potential association with cardiac and extracardiac (EC) abnormalities and chromosomal defects [4].

The incidence of the RAA is relatively low, about 0.1% in low-risk pregnancies [2, 5–7]. It is one of the least diagnosed congenital heart disease [2], probably because

of its isolated nature [8] and the apparent normal “V” sing when both the aortic arch and the *ductus arteriosus* (DA) are to the right of the trachea (type I RAA). However, the diagnosis of this aberrant branching is reported as feasible [3, 9], based on the systematic evaluation of the three vessels and trachea (3VT) view, part of the cardiac sweep that is recommended during the routine pregnancy anomaly scan [10, 11].

The antenatal diagnosis of RAA is important, due to the potential associated abnormalities and the complications it can trigger, esophageal and tracheal compressions with dyspnea and dysphagia [6]. It appears important to recognize the RAA type to properly counsel the couple regarding the pregnancy outcome [9].

Aim

The aim of this study was to review and evaluate the fetuses diagnosed in our Center with RAA in the past 10 years. We took into consideration the association of

RAA with other congenital anomalies and chromosomal defects when evaluating the outcome of the pregnancy. These data are important to help practitioners counsel correctly and balanced the parents when the fetus is diagnosed with a certain type of RAA. The second purpose of the study was to determine the incidence of RAA and its subtypes in our Center, over a long period of time, and associate the pregnancy outcome with these anatomical types. The literature report wide variations for incidence rates and variable outcomes depending on the type of RAA. Therefore, the present study emphasizes the incidence and prognosis of each type separately. In conclusion, we conducted an evaluation of the outcome in relation with the type of RAA, given the controversial prognosis for some RAA cases, especially type I [12].

Embryology and types of RAA

The normal aortic arch is orientated posteriorly and to the left of the trachea, and together with DA form the well-known “V” sign on the 3VT plane discussed earlier. Classically, the RAA is defined by a “U” sign formed by the transverse view of the aortic arch, heading to the right of the trachea, and meeting the left DA behind the trachea. This appearance in the absence of the “V” sign raise a great suspicion of an aortic arch anomaly, more exactly, a RAA [13].

In 1948, Jesse E. Edwards, an American cardiologist, introduced a theory which states that all aortic arch anomalies are caused by disruptions in the embryonic formation of the five pairs of pharyngeal arches [14]. These arches are the origin of most of the head, neck and thorax arteries, including the aortic arch, the subclavian arteries and the carotid arteries [13]. The embryological arterial system consists of five pairs of primordial pharyngeal arches. Each arch associates a cranial nerve and an artery. The aortic arches arise from the aortic sac and they are situated in the mesenchyme of the pharyngeal arches. These five pairs of aortic arches are numbered

I, II, III, IV and VI because the Vth pair never develops or regresses early on. During embryological development, the disposition of these symmetrical arteries changes and some of these vessels disappear completely [15].

The aortic arch evolves from the 4th pair of aortic arches and the pulmonary arteries – from the 6th pair. A connection appears between the two primitive aortas that form the 4th arch and the pulmonary arch, on both sides, known as the left and the right DA. The two primitive aortas form a ring around the trachea and esophagus. A second ring around these structures is formed by the left and right DA. This is the normal embryological arterial system and disruptions at this level will lead to congenital heart and great vessels anomalies [16]. In normal development, the right arch regresses and become the origin of the right subclavian artery. The left side will form the aortic cross. The right DA regresses and the left DA remains functional during fetal life and will become the arterial ligament after birth [15].

A RAA develops when the right side of the 4th pair of aortic arches persists and it can be classified in three categories (Figure 1) – RAA with mirror image branching (right DA, type I – “V” sign), RAA with left DA (type II – “U” sign), and double aortic arch (DAA). The first type of RAA is characterized by the involution of the left arch and the persistence of the right one which communicates with the pulmonary trunk through the right DA and forms a “V” sign on the 3VT view to the right of the trachea, hence the name of this type. The difference between type I and type II of RAA is that in type II the communication between the aortic arch and the pulmonary trunk is made through the left DA which persists as the right DA involutes. The confluence of the RAA associated with a left DA will appear as a “U” sign in the 3VT plane. In the DAA, both right and left aortic arches persist as a vascular ring around the trachea and esophagus with either the left or the right, or even both DA [9].

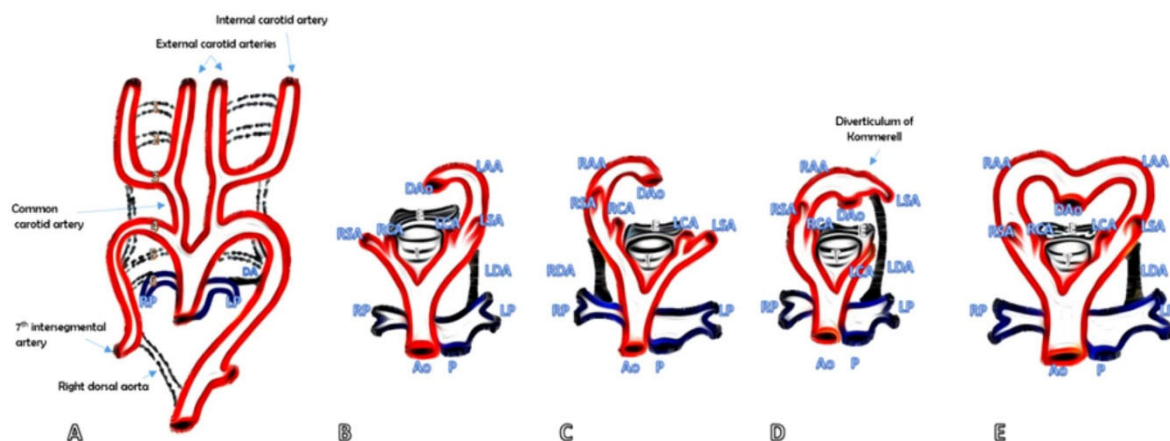


Figure 1 – (A) Normal embryological development and involution (with dotted lines) of the six pairs of aortic arches (noted with Nos. from 1 to 6); (B) Normal LAA with LDA; (C) RAA with RDA – type I; (D) RAA with LDA forming Kommerell's diverticulum – type II; (E) DAA surrounding the trachea and esophagus. Ao: Aorta; DA: Ductus arteriosus; DAA: Double aortic arch; DAo: Descending aorta; E: Esophagus; LAA: Left aortic arch; LCA: Left common artery; LDA: Left ductus arteriosus; LP: Left pulmonary artery; LSA: Left subclavian artery; P: Pulmonary trunk; RAA: Right aortic arch; RCA: Right common artery; RDA: Right ductus arteriosus; RP: Right pulmonary artery; RSA: Right subclavian artery; T: Trachea.

Chromosome anomalies associated with RAA

RAA is often associated with chromosomal anomalies. The most frequent genetic anomaly is the 22q11.2 deletion, which is specific for DiGeorge syndrome [17]. Thus, microarray-based comparative genomic hybridization (aCGH) is the preferred genetic testing method, that offers more information than the classical karyotype and diagnostic for the 22q11.2 deletion [17–19]. A small thymus, which accompanies RAA, is also marker for genetic anomaly, particularly the 22q11.2 deletion [17].

Patients, Materials and Methods

The obstetrical databases of the tertiary center from Romania (Emergency County Hospital of Craiova) were retrospectively reviewed for fetal morphological assessments during a 10-year period (2012–2020). The indications for the fetal scans were: first or second trimester routine anatomy scans, cases referred for suspected cardiac or EC anomalies, and routine scans with other indications. There were approximately 10 500 pregnant women examined in this period of time and our team discovered 18 RAA cases.

The study group

The study group consisted of 18 cases of RAA diagnosed by fetal echocardiography. Ultrasound (US) examinations were performed using GE Voluson Pro, Expert, E8 and E10 systems equipped with 4–8 MHz curvilinear transducers and Philips EPIQ 7 system with the following transducers: eL18-4 linear array 18–4 MHz, C9-2 curved array 9–2 MHz, and V6-2 convex three-dimensional (3D) array 6–2 MHz. Transvaginal examination with a 5–9 MHz curvilinear transducer was performed additionally, when was necessary for better visualization of fetal anatomy or abnormalities. The classical grey scale mode combined with color, power and pulsed-wave Doppler modes were used for a detailed fetal anatomy and heart assessment, according to a comprehensive protocol previously published by our Center [20–25]. During the cardiac sweep, 3VT view was used to identify the laterality of the aortic arch and of the DA in relation to the trachea and the spine, and thus, for RAA classification type. Two cases that fulfilled these criteria were excluded, as they associated dextrocardia and *situs inversus*, respectively.

The fetal characteristics that were observed included associated intracardiac (IC) and EC anomalies and the presence of genetic anomalies, in particular the 22q11.2 deletion. Moreover, the outcome of the pregnancy, whether alive and well neonate or the medical termination of pregnancy (TOP) was noted. Postnatal confirmation of the diagnosis and the evolution of the infant, especially the compressive symptoms, were recorded for the fetuses that were born alive. Fetal autopsy was proposed in TOP

cases, to confirm the suspected anomalies [26]. The study received the Ethics Committee approval, and all participants were given explicit details regarding the study and offered their consent.

The evaluation protocols

The 3VT plane represents a standard view of the cardiac sweep for every fetus examined in our Center both in first and second trimester. This view, along with the correct identification of the heart apex orientation at the level of four-chamber view, offers an easy confirmation of the heart, aortic arch, and DA laterality.

The heart investigation protocol is not limited to the 3VT view. First trimester heart evaluation relies mostly on cardiac sweep color Doppler investigation. A full Doppler cardiac sweep assesses the atrioventricular flows, the aortic flow emerging from the left ventricle, the pulmonary flow emerging from the right ventricle and their trajectory to the left of the spine. We routinely visualize and sample *ductus venosus* and tricuspid valve flows using pulsed Doppler [27, 28]. We routinely relay on grey scale US scan to evaluate the situs of the heart and the offsetting of the atrioventricular valves. This protocol is feasible in the first trimester and we recommend this approach to every pregnancy [20, 29]. An extended or detailed first trimester protocol ensures an accurate diagnosis of the laterality of the aortic arch and most of the major congenital heart diseases. The fetal heart was evaluated in the second or third trimester, according to the published guidelines [10].

The first trimester anatomy scan includes broad US protocols applied to all anatomical structures. The reason of this approach is to diagnose the IC and EC anomalies as early as possible and give parents time to acknowledge the information and the practitioner to further investigate and confirm the suspicions.

Genetic testing

All couples were offered genetic counselling following RAA diagnosis. The genetic tests offered to the parents who accepted these investigations were: karyotyping, quantitative fluorescence-polymerase chain reaction (QF-PCR) and aCGH.

Results

There were 18 fetuses included in the study, 16 singleton fetuses and two fetuses from two twin pregnancies. The study group is presented in (Table 1). The incidence of the RAA in our Center was 0.17%.

This incidence was calculated over a period of 10 years that included approximately 10 500 fetal scans. The mean gestational age (GA) at the diagnosis was 16 weeks (with a range between 12 and 28 gestational weeks (Table 2).

Table 1 – Summary of the cases

No.	Year	GA at diagnosis [weeks]	RAA type	IC anomalies	EC anomalies	Genetic testing	Outcome	Comments
1.	2011	12	I	TOF		Normal karyotype Normal aCGH	TOP	Confirmed at autopsy
2.	2012	20	II		Hypoplastic nasal bone Small vitelline vesicle in first trimester Thymus hypoplasia	22q11.2 deletion Normal karyotype	TOP	Cranio-cerebral dysmorphism Confirmed at autopsy

No.	Year	GA at diagnosis [weeks]	RAA type	IC anomalies	EC anomalies	Genetic testing	Outcome	Comments
3.	2012	13	I	TOF		Multiple microdeletions Normal karyotype Normal aCGH	TOP	Confirmed at autopsy
4.	2012	22	II		Septo-optic dysplasia	Normal karyotype Normal aCGH	Live birth	Postnatal confirmation <i>Twin pregnancy</i>
5.	2012	13	I			Normal karyotype Normal aCGH	Live birth	Normal phenotype
6.	2013	13	II	AVSD		Normal karyotype Normal aCGH	TOP	Confirmed at autopsy
7.	2013	13	DAA			Normal karyotype Normal aCGH	Live birth	Postnatal confirmation
8.	2014	13	II			Normal karyotype Normal aCGH	Live birth	Postnatal confirmation <i>Twin pregnancy</i>
9.	2015	18	II		Cystic hygroma, left diaphragmatic hernia, long bones hypoplasia	Trisomy 18	TOP	Confirmed at autopsy
10.	2016	12	II			Normal karyotype Normal aCGH	Live birth	Postnatal confirmation, favorable evolution
11.	2017	21	I			Normal karyotype Normal aCGH	Live birth	Normal phenotype
12.	2017	22	I	TOF	Thymus hypoplasia	<i>22q11.2 deletion</i> Normal karyotype	TOP	Confirmed at autopsy
13.	2017	22	II		Esophageal atresia, duodenal atresia	47,XY,+mar[15]/46,XY[38] mosaicism	Live birth	Postnatal confirmation. Surgical repair of esophageal atresia, duodenal atresia and anal atresia, normal phenotype
14.	2018	22	DAA		Thymus hypoplasia	<i>22q11.2 deletion</i> Normal karyotype	TOP	Confirmed at autopsy
15.	2018	28	II	Right atrial isomerism, AVSD, DORV, PLSVC	IUGR, median-sided stomach, left-sided gallbladder	NK	Live birth	Postnatal confirmation of RAA, right-sided heart, right-sided stomach, middle sided liver, no spleen, LAFB, favorable postnatal evolution
16.	2018	22	II	TOF		<i>22q11.2 deletion</i> Normal karyotype	Live birth	Postnatal confirmation, surgery for TOF, favorable postnatal evolution
17.	2019	12	II			Normal karyotype Normal aCGH	Live birth	Postnatal confirmation, favorable evolution
18.	2019	13	II	AVSD, CAT	SUA, mesomelia, acromelia, cerebral ventriculomegaly, ectopic kidney	Normal karyotype Normal aCGH	TOP	Confirmed at autopsy

aCGH: Microarray-based comparative genomic hybridization; AVSD: Atrioventricular septal defect; CAT: Common arterial trunk; DAA: Double aortic arch; DORV: Double outlet right ventricle; EC: Extracardiac; GA: Gestational age; IC: Intracardiac; IUGR: Intrauterine growth restriction; LAFB: Left anterior fascicular block; NK: Not known; PLSVC: Persistent left superior vena cava; SUA: Single umbilical artery; TOF: Tetralogy of Fallot; TOP: Termination of pregnancy.

Table 2 – General characteristics of the study group. Association with structural and genetic abnormalities

Characteristic		Value n (%)
GA at diagnosis		Mean GA: 16 weeks (range: 12–28 weeks)
Total		7/18 (38.89%)
IC anomalies	TOF	4/18 (22.23%)
	Other anomalies	3/18 (16.67%)
EC anomalies		8/18 (44.44%)
Total		7/17 (41.17%)
Genetic anomalies	<i>22q11.2 deletion</i>	4/17 (23.53%)
	Other anomalies	3/17 (17.65%)
Outcome	TOP	8/18 (44.45%)
	Live birth	10/18 (55.55%)

EC: Extracardiac; GA: Gestational age; IC: Intracardiac; n: No. of cases; TOF: Tetralogy of Fallot; TOP: Termination of pregnancy.

All the RAA fetuses examined in the first trimester were accordingly diagnosed with RAA, as the diagnosis was confirmed at the mid trimester anomaly scan or fetal autopsy. No false positive diagnoses were recorded. Around 8% of the anomaly scan cases examined in our Center were referred from other Centers for second opinion, because an anomaly was suspected. Therefore, we cannot consider our group a low-risk population. One patient from our group was referred from another Center for a suspected cardiovascular anomaly, representing about 5% of the cases. Prenatal diagnosis of RAA was confirmed in all 18 fetuses, postnatally or at the autopsy, with no false positive diagnoses. We cannot calculate the false negative rate because we did not search systematically postnatally the presence of the anomaly in our study group. However, we are not aware of RAA diagnoses in neonates or children classified as normal during the prenatal anomaly scan.

Detection rate associated with the GA

GA of the first presentation in our Center coincides with the GA of the diagnosis of the RAA (Table 2). There were nine (50%) cases detected at the first trimester anomaly scan (12–13 gestational weeks). Eight (44.45%) cases presented themselves for the first time in our Center for the second trimester anatomy scan or were referred from other Centers for suspected anomalies (18–24 gestational weeks). There were no fetuses confirmed with a normal aortic arch at the first trimester anatomy scan and the diagnose refuted at the mid trimester anatomy scan. The last case (5.55%) was diagnosed in the third trimester. The latter case had no medical care during the pregnancy and presented at 28 gestational weeks in the Emergency Room for uterine contractions.

Table 3 – The distribution of RAA types in our study group in association with IC, EC and genetic anomalies and the outcome of the pregnancies

RAA type	Value n (%)	IC anomalies / TOF n (%)	EC anomalies n (%)	Genetic anomalies / 22q11.2 del n (%)	TOP n (%)	Live births n (%)
Type I	5/18 (27.78%)	3/5 (60%) / 3/5 (60%)	1/5 (20%)	2/5 (40%) / 1/5 (20%)	3/5 (60%)	2/5 (40%)
Type II	11/18 (61.12%)	4/11 (36.37%) / 1/11 (9.09%)	6/11 (54.55%)	4/10 (40%) / 2/10 (20%)	4/11 (36.36%)	7/11 (63.64%)
DAA	2/18 (11.10%)	0/2 (0%)	1/2 (50%)	1/2 (50%) / 1/2 (50%)	1/2 (50%)	1/2 (50%)

DAA: Double aortic arch; EC: Extracardiac; IC: Intracardiac; n: No. of cases; RAA: Right aortic arch; TOF: Tetralogy of Fallot; TOP: Termination of pregnancy.

The general characteristics of the study group, concerning the associated structural and genetic anomalies and the outcome of the pregnancies are presented in Table 2. Seven cases (38.89% of all RAA cases) associated IC anomalies [tetralogy of Fallot (TOF), atrioventricular septal defect (AVSD), right atrial isomerism, double outlet right ventricle (DORV), persistent left superior vena cava (PLSVC) and common arterial trunk (CAT)]. Four fetuses were diagnosed with TOF (22.23% of all RAA cases). EC anomalies were present in 44.44% of all RAA cases (hypoplastic nasal bone, septo-optic dysplasia, cystic hygroma, left diaphragmatic hernia, long bones hypoplasia, thymus hypoplasia, esophageal atresia, duodenal atresia, median stomach position, left-sided gallbladder, single umbilical artery (SUA), mesomelia, acromelia, cerebral ventriculomegaly, ectopic kidney).

The outcome of RAA with right DA

In the type I subgroup, three (60%) cases were associated with TOF. No other IC anomalies were associated with this type of RAA and just one case (25% of type I) associated an EC anomaly, thymus hypoplasia. This fetus is the only one in our study group diagnosed with thymus hypoplasia and it also associated TOF and 22q11 deletion. The three pregnancies that associated fetal RAA with right DA (type I), TOF and 22q11.2 deletion were terminated, while two fetuses with type I RAA, normal genetics and morphology scan were born alive and had a good evolution postpartum. We present a case of type I RAA (Figure 2).

The incidence of RAA in our medical Center

As mentioned before, the incidence of RAA in our Center was 0.17%. We present the distribution of RAA types in our study group and the association with IC and EC anomalies, genetic anomalies, and the outcome of the pregnancies according to the RAA three types (Table 3).

The study group was divided according to the type of RAA: five cases (27.78% of the total cases) were diagnosed with type I RAA, 11 (61.12%) cases with type II RAA, and two (11.10%) cases with DAA.

Therefore, the most frequent type of RAA in the study group was type II, characterized by a RAA and left DA.

The pregnancy outcome in cases with RAA and left DA

In type II subgroup, four cases (36.37% of type II) associated other heart anomalies (AVSD, right atrial isomerism, DORV, PLSVC, TOF, CAT). AVSD was present in three of these four cases and TOF was diagnosed in one case. Six fetuses (54.55% of type II) presented EC anomalies (hypoplastic nasal bone, septo-optic dysplasia, cystic hygroma, left diaphragmatic hernia, long bones hypoplasia, esophageal atresia, duodenal atresia, median-sided stomach, left-sided gallbladder, SUA, mesomelia, acromelia, cerebral ventriculomegaly, ectopic kidney, thymus hypoplasia). Ten cases were tested genetically and four (40%) of them were diagnosed with a chromosomal anomaly (two cases of 22q11.2 deletion, one case of trisomy 18 and one case of 47,XY,+mar[15]/46,XY[38] mosaicism). The rate of live births in this group was 63.64% and of TOP 36.3%. In one case (No. 15, Table 1), parents declined invasive testing, at 28 gestational weeks. We present a case of type II RAA (Figure 3).

The anomalies and prognosis associated with DAA

DAA was the least common form of RAA in the study group, with only two cases diagnosed during this time interval. None of the cases associated other IC anomalies. One case presented thymus hypoplasia. Both of the fetuses underwent prenatal invasive diagnosis and one of them was diagnosed with 22q11.2 deletion. This

pregnancy associated thymus hypoplasia and was terminated. The other couple gave birth to a live neonate with a normal phenotype and a good neonatal evolution. A case of DAA is presented in Figure 4.

Genetic testing in RAA cases

Genetic testing was offered to all affected pregnancies and was accepted in 17 cases (Table 1). Chromosomal anomalies were found in 41.17% of the tested cases and the most frequent anomaly was the 22q11.2 deletion (DiGeorge syndrome) – in 23.53% of the tested cases.

The outcome of the pregnancies depending on the RAA type

The general outcome of the pregnancies is presented in Table 1. Parents chose medical TOP in 44.45% of the RAA cases. The indications of TOP were as following: TOF in three cases (one of them associated 22q11.2 deletion), one case of trisomy 18, one case of DAA associated with thymus hypoplasia and 22q11.2 deletion and three cases that associated IC and/or EC anomalies (22q11.2 deletion was present in one case). Isolated RAA (iRAA) was not terminated and had a good postnatal outcome.

The rest of 55.55% of pregnant women gave birth to neonates that had a good postnatal evolution.

The distribution of the TOP cases according to the RAA type was: three cases of type I (60% of the total type I cases and 37.50% of the total TOP cases), four cases of type II (36.37% and 50% respectively) and one case of DAA (50%, 12.50% respectively).

We present the genetic anomalies and structural (cardiac and EC) malformations associated with RAA type and the correlation with the outcome. 22q11.2 deletion plays an important role in the diagnosis and management of these cases; thus, the distribution of this deletion was studied individually (Figure 5). We considered RAA as iRAA when neither structural nor genetic anomalies were associated.

iRAA was observed in six cases, while 12 cases presented other IC and/or EC anomalies. No fetus with an iRAA had chromosomal anomalies. However, seven cases of chromosomal anomalies were diagnosed in fetuses that associated other structural anomalies. Five of these cases were terminated and the other two gave birth to neonates with normal phenotypes and a good postnatal evolution.

No iRAA cases with normal karyotype were terminated. There were six cases of iRAA and all of the fetuses were born alive and had a good postnatal outcome. The three cases that were terminated associated severe structural anomalies.

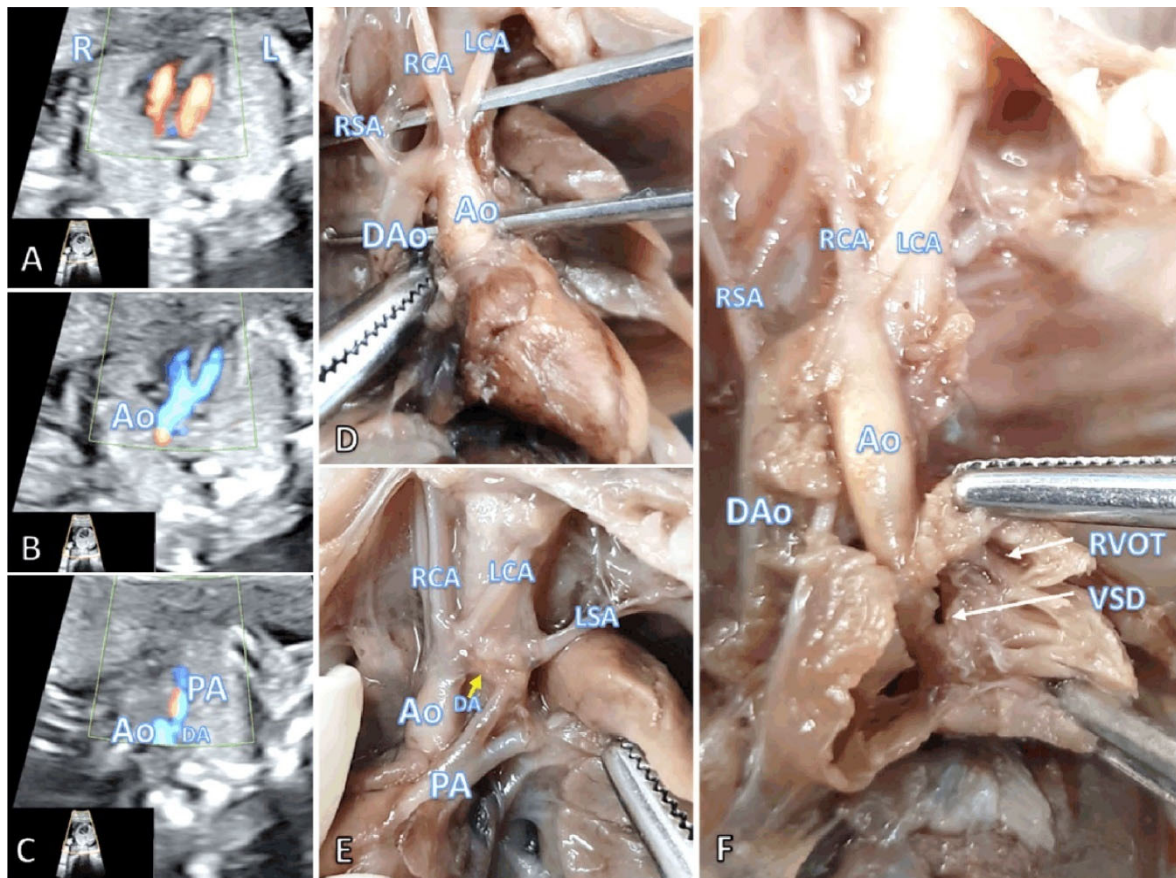


Figure 2 – Presenting Case No. 12 (Table 1) – type I RAA case with right DA and cardiac anomaly: (A) Ultrasound directional power Doppler, four-chamber view; (B) VSD with overriding aorta; (C) RAA with right DA; (D) Pathology examination – RAA; (E) Right DA; (F) Heart dissection – VSD. Ao: Aorta; DA: Ductus arteriosus; DAA: Descending aorta; L: Left; LCA: Left carotid artery; LSA: Left subclavian artery; PA: Pulmonary trunk; R: Right; RAA: Right aortic arch; RCA: Right carotid artery; RSA: Right subclavian artery; RVOT: Right ventricular outflow tract; VSD: Ventricular septal defect.

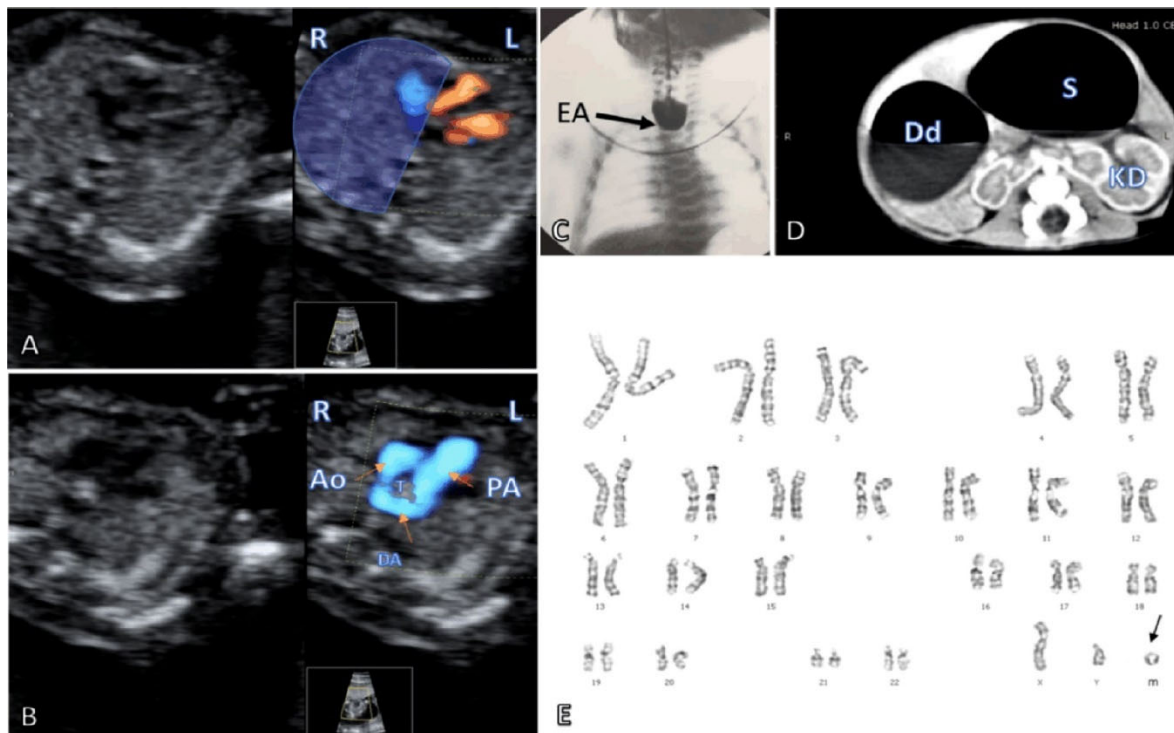


Figure 3 – Presenting Case No. 13 – type II RAA case with a good postpartum evolution following surgical correction of associated abnormalities: (A) Ultrasound duplex mode – grey scale and directional power Doppler, four-chamber view, showing normal situs, area and axis of the heart; (B) RAA and left DA, connected by the Kommerell's diverticulum appear as a “U”-shaped vascular ring around the trachea and esophagus – “U” sign; (C) First day postpartum radiography showing esophageal pouch (esophageal atresia was confirmed); (D) Postpartum CT for esophageal atresia management reveals dilated stomach and duodenum – “double bubble” sign, suggesting duodenal atresia and horseshoe kidney; (E) 47,XY,+mar – normal karyotype with chromosome marker. Ao: Aorta; CT: Computed tomography; DA: Ductus arteriosus; Dd: Duodenum; EA: Esophageal atresia; KD: Kidney; L: Left; PA: Pulmonary trunk; R: Right; RAA: Right aortic arch; S: Stomach; T: Trachea.

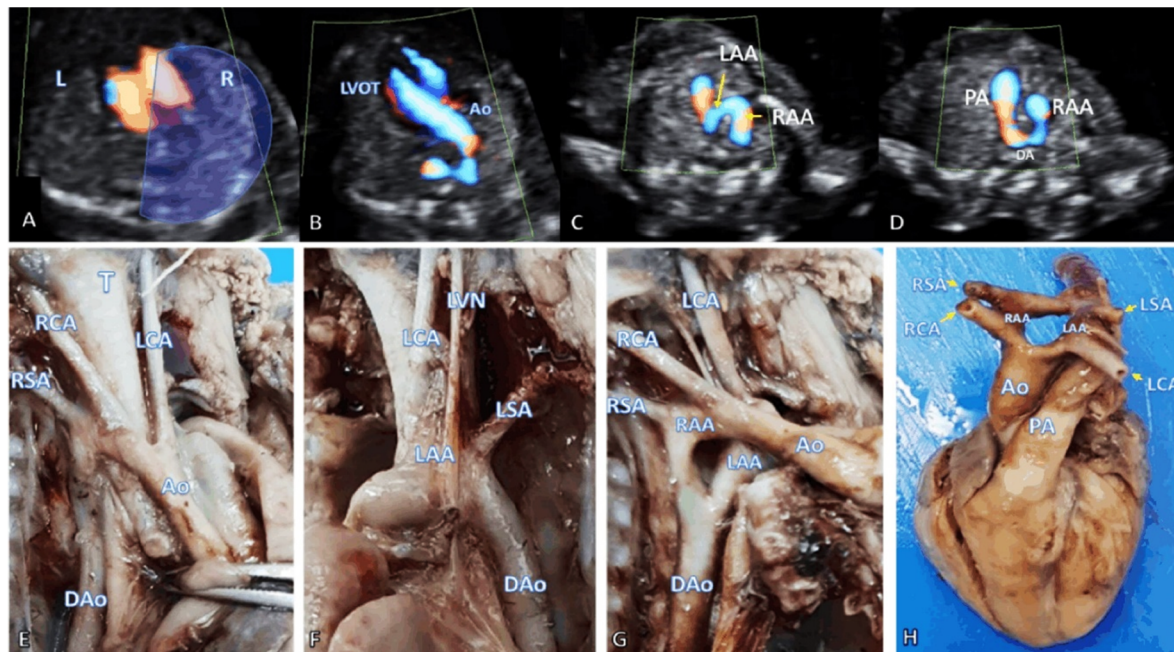


Figure 4 – DAA in a second trimester pregnancy termination (Case No. 14). Ultrasound cardiac sweep with high-definition directional power Doppler mode: (A) Four-chamber view, with normal cardiac situs; (B) Left ventricular outflow tract plane, with aorta emerging from the left ventricle and coursing to the right of the spine; (C) Right ventricular outflow tract plane (pulmonary artery) and a DAA is identified in the three vessels plane, with a narrower left aortic arch; (D) Left-sided DA. Pathology examination: (E) RAA view with emergent vessels; (F) Left aortic arch with emergent vessels; (G) Vascular ring formed by the two arches; (H) Heart isolation with DAA and emergent vessels of each arch. Ao: Aorta; DA: Ductus arteriosus; DAA: Double aortic arch; DAo: Descending aorta; LCA: Left carotid artery; LSA: Left subclavian artery; LVN: Left vagus nerve; PA: Pulmonary trunk; RAA: Right aortic arch; RCA: Right carotid artery; RSA: Right subclavian artery; T: Trachea.

Total cases 18 cases		
Normal karyotype Normal aCGH 10 cases One case without genetics (*)	Genetic anomalies 7 cases	
	22q11.2 deletion 4 cases	Other anomalies 3 cases
Type I iRAA TOP Live birth 2 cases with IC and/or EC anomalies TOP Live birth	Type I iRAA TOP Live birth with IC and/or EC anomalies TOP one case Live birth	Type I iRAA TOP Live birth with IC and/or EC anomalies TOP one case Live birth
Type II iRAA TOP Live birth 3 cases with IC and/or EC anomalies TOP 3 cases Live birth 2 cases (*)	Type II iRAA TOP Live birth with IC and/or EC anomalies TOP one case Live birth one case	Type II iRAA TOP Live birth with IC and/or EC anomalies TOP one case Live birth one case
DAA iRAA TOP Live birth one case with IC and/or EC anomalies TOP Live birth	DAA iRAA TOP Live birth with IC and/or EC anomalies TOP one case Live birth	DAA iRAA TOP Live birth with IC and/or EC anomalies TOP Live birth

Figure 5 – Distribution of the genetic anomalies and IC/EC malformations and association with the outcome of the pregnancies. aCGH: Microarray-based comparative genomic hybridization; DAA: Double aortic arch; EC: Extracardiac; IC: Intracardiac; iRAA: Isolated right aortic arch; TOP: Termination of pregnancy.

☒ Discussions

The incidence of RAA in general population and in low-risk pregnancies is estimated between 0.058% and 0.18% [2, 3, 13, 30–33]. However, there are studies made on high-risk groups that report a higher incidence, 0.35% [34] – 0.5% [35]. In our study group, which can be considered of intermediate risk because of the referred cases, the incidence was 0.17% a value that is in line with published literature and supports the accuracy of the diagnosis. The diagnosis can be easily established during the cardiac scan on the 3VT view starting with the late first trimester genetic and anomaly scan [12, 24]. We diagnosed nine cases of RAA at the first trimester anatomy scan and all cases were confirmed at the second trimester scan or pathology examination following TOP. Of this group, there were no cases missed, diagnosed later in pregnancy, postpartum or at the pathology examination.

The incidence of each type of RAA was type I – 27.78%, type II – 61.12%, and DAA – 11.10%. This distribution has a great importance because there are some differences between large studies. Some studies did not report type I cases [36], while some other studies report a ratio between the three types of RAA was in favor of type I, between 45% and 62.5% of all aortic arch anomalies [3, 37]. Most of the studies report an incidence for type I between 7% and 17% [33–35, 38]. In our study group, they represented about a quarter (27.78%) of the cases. An explanation for the higher incidence in our study could be the “V”-shaped appearance of this anomaly that resembles with the normal confluence of arterial arches in the 3VT plane, used for US diagnosis. Only the laterality of the “V” sign is different in type I RAA, while in type II RAA and DAA there is no resemblance with the normal aspect. This may lead to type I RAA underdiagnose during prenatal scan and a consecutive underestimation of its rate.

Traditionally, type I RAA is considered almost always associated with cardiac abnormalities [39]. However, it was later proved that RAA with RDA may be found isolated in fetuses with normal outcome [12]. Later studies reported wide variations of abnormal associations of this condition: a 30% to 90% risk of severe congenital heart defects [5, 9, 32, 37], namely TOF in 13% to 77% cases [9, 37, 40] and a 1% to 15.38% risk of 22q11.2 deletion [5, 37]. In our study, three cases were associated with TOF (60%), one case with thymus hypoplasia and one case came out positive for 22q11.2 deletion and another case for multiple microdeletions. Our data suggest that the risk for DiGeorge syndrome in our study group was 20% for type I RAA. Thus, our study supports the previous data which suggest that a RAA with a right DA has a higher risk of associated complex heart disease and DiGeorge syndrome [9, 13].

Type II RAA cases were reported in previous studies accompanied by severe heart defects in a variable proportion, between 8.3% and 72%, depending on the population risk [3, 9, 31, 35, 40, 41]. However, the usual reported incidence of major heart anomalies is about 10% [9, 40]. In our cohort, which should be considered of intermediate risk, the incidence of associated heart defects in this subgroup was 36.37% and should be taken into consideration because the cardiac anomalies associated were severe (TOF, right atrial isomerism, DORV, PLSVC and CAT). We suggest a careful cardiovascular evaluation in fetuses with this condition. The reasons for our higher rate of associated anomalies may be explained by under-reported RAA in cases of congenital heart disease, where the major heart anomaly was mainly studied and reported. We do not believe that we missed type II RAA cases, as the 3VT view was mandatory in all evaluations, where the presentation of this condition is very characteristic. Also, we did not encounter missed RAA cases during the follow-up evaluations. However, the relatively small number of cases from our series may represent a source of errors. Concerning EC anomalies, 54.55% type II cases associated variable degrees of malformations. However, these were not a direct indication for TOP in none of the cases.

Overall, the outcome of type II RAA was better than type I RAA cases, given the lower rate of cardiac, severe EC and genetic abnormalities. However, although the RAA type was considered an important factor for prognosis, our data show that the association of significant structural or genetic anomalies represents the main prognostic factor for pregnancy outcome.

The general incidence of IC anomalies and TOF in our study group was 38.89% and 22.23%, respectively (for the entire group). The most frequent anomalies were TOF and AVSD. Our findings are in accordance with the literature, as a large cohort study of 98 fetuses showed an incidence of IC anomalies stratified as following: 56.12% conotruncal anomalies, 36.73% TOF and 8.16% septal defects [41]. TOF is reported in other studies in 5.6% to 25% RAA cases [3, 6, 36].

Concerning EC anomalies incidence, we found ranges

between 2% and 38.89% [6, 31, 35, 41] in the literature. The incidence of EC anomalies in our study group was 44.44%. Some of the most common EC anomalies associated with RAA are gastrointestinal malformations [8, 35, 42] and this finding is supported by our study as well (left diaphragmatic hernia, esophageal atresia, duodenal atresia, right-sided stomach, left-sided gallbladder).

Another important aspect is represented by the symptomatology secondary to vascular compression. DAA is the most common cause of tracheal and esophageal compression of aortic origin [43]. The rate of symptomatic neonates varies between 41% and 98% in different studies [34, 44]. In our study group, only one case of isolated DAA was born alive and the neonate did not develop compression symptoms in the neonatal and early childhood period. Compression symptoms can be caused by type II as well, 5% type II being associated with Kommerell's diverticulum [3, 41, 45]. Some authors consider the "U" sign always associated with a vascular ring [6]. In our group, no neonates developed these symptoms, and none needed surgery for a vascular ring. We should be aware of these conditions, as symptoms may occur in the first 24 months of life, in 25.2% of the cases where a vascular ring is present [8]. Our data suggest that the rates of respiratory and digestive complications due to RAA vascular rings may be lower than reported, at least in early infancy. Also, symptoms might occur in adulthood due to atherosclerotic changes [46, 47].

One study found an incidence of the 22q11.2 deletion in iRAA cases (no other IC or EC anomalies) of 8.5%, increasing to 25% in the presence of another sonographic anomaly and to 100% when the thymus was hypoplastic or absent. The same study emphasizes an association of 90% of RAA with a small or non-visible thymus in the 22q11.2 deletion cases [17]. In our study group, three cases had a hypoplastic thymus and all of them associated 22q11.2 deletion. One of the cases associated type I RAA, TOF and 22q11.2 deletion. All three couples opted for TOP and fetopathology evaluation confirmed the anomalies. The incidence of thymus hypoplasia in our cohort was 16.67%.

In terms of abnormal genetic associations, in our study group 17/18 cases were tested for genetic disorders. All types of chromosomal anomalies and specifically 22q11.2 deletion were present in 41.17% and 23.53%, respectively, in the tested group (17 cases). These values range from 9% to 42.8% for chromosomal anomalies and between 6.1% and 28.5% for 22q11.2 deletion [8, 31, 33] in other studies. Moreover, some authors consider that the of association between RAA and 22q11.2 is influenced by the presence of other IC and EC anomalies: 8% to 24% in isolated cases and 24% to 46% in cases that associated other IC and EC anomalies [17, 35, 48, 49].

In agreement with previous recommendations [50, 51] and based on our results, we recommend genetic testing for 22q11.2 deletion specifically or by means of aCGH for all pregnancies diagnosed with a RAA (isolated or not), even if some authors do not consider this investigation in isolated cases [52]. Some authors

consider iRAA to even have a higher risk for chromosomal anomalies [18], but this approach cannot be validated by the results of our study.

In our study group, almost half of the pregnancies were terminated for major structural or genetic abnormalities (44.45%) representing 60% type I, 36.36% type II, and 50% DAA. The rest of the fetuses were born at term and had a good neonatal outcome. No neonates required surgery for the aortic arch anomaly, but some of them underwent interventions for the associated anomalies (TOF, digestive malformations). The rate of TOP was higher in our group (due to the associated anomalies), but the postnatal outcome of the newborns with RAA was good, with no compressive symptoms reported and a low rate of neonatal surgeries. There were no intrauterine or postpartum demises. Other authors communicated a lower TOP rate, 6.12%, but combined with a high rate of *in utero* death, 4% and postpartum – 10.20% [41]. Other authors reported TOP between 8.34% and 19%, and a good evolution for most of the live births [3, 8, 36].

The information provided by our study is important for the practitioner in order to advise the couple towards a correct decision. When RAA is diagnosed, an extended scanning protocol for IC and EC anomalies should be implemented indifferent the anatomical type and parents should be offered invasive prenatal testing. Special care should be provided to DAA and type I RAA, as the rate of major anomalies appears higher in these cases.

☒ Conclusions

RAA is an uncommon disorder, frequently associated with IC and EC malformations and chromosomal anomalies, indifferently the anatomical type. Prenatal detection of this pathology is facile if the 3VT plane is systematically evaluated during cardiac sweep, starting from the first trimester anatomy scan. RAA detection should trigger detailed anatomy scan and genetic evaluation, with special attention to TOF and 22q11 deletion. Similar figures were registered regarding the outcome of the pregnancies, as almost half ended up in pregnancy termination due to structural or genetic abnormalities (44.45%). When isolated, RAA associates a good outcome, indifferently the anatomical type. Although the RAA type was considered an important factor for prognosis, our data show that the association of significant structural or genetic anomalies represents the main prognostic factor for pregnancy outcome. An apparently iRAA may associate genetic anomalies, particularly the deletion responsible for DiGeorge syndrome, justifying the need for prenatal invasive testing for all cases suspected with RAA or DAA. To conclude, the outcome of fetuses diagnosed prenatally with RAA depends on the associated anomalies and cannot be estimated without extended scans and genetic testing. Although the number of patients in this study is relatively low and hinders the possibility of a conclusive prognosis, the data from this current study, corroborated with the already published literature, offers a well-founded argument that all RAA fetuses, isolate or not, should be offered prenatal invasive karyotyping and

22q11.2 deletion analyze. When isolated, RAA or DAA has usually a good outcome and do not require surgery.

Conflict of interests

The authors declare that they have no conflict of interests.

Authors' contribution

Ana-Maria Petrescu and Dan Ruican equally contributed to this article.

References

- [1] Schleich JM. Images in cardiology. Development of the human heart: days 15–21. *Heart*, 2002, 87(5):487. <https://doi.org/10.1136/heart.87.5.487> PMID: 11997429 PMCID: PMC1767109
- [2] Achiron R, Rotstein Z, Heggesh J, Bronshtein M, Zimand S, Lipitz S, Yagel S. Anomalies of the fetal aortic arch: a novel sonographic approach to *in-utero* diagnosis. *Ultrasound Obstet Gynecol*, 2002, 20(6):553–557. <https://doi.org/10.1046/j.1469-0705.2002.00850.x> PMID: 12493043
- [3] Galindo A, Nieto O, Nieto MT, Rodríguez-Martín MO, Herraiz I, Escribano D, Granados MA. Prenatal diagnosis of right aortic arch: associated findings, pregnancy outcome, and clinical significance of vascular rings. *Prenat Diagn*, 2009, 29(10): 975–981. <https://doi.org/10.1002/pd.2327> PMID: 19603384
- [4] McElhinney DB, Clark BJ 3rd, Weinberg PM, Kenton ML, McDonald-McGinn D, Driscoll DA, Zackai EH, Goldmuntz E. Association of chromosome 22q11 deletion with isolated anomalies of aortic arch laterality and branching. *J Am Coll Cardiol*, 2001, 37(8):2114–2119. [https://doi.org/10.1016/s0735-1097\(01\)01286-4](https://doi.org/10.1016/s0735-1097(01)01286-4) PMID: 11419896
- [5] Cavoretto PI, Sotiriadis A, Girardelli S, Spinillo S, Candiani M, Amodeo S, Farina A, Fesslova V. Postnatal outcome and associated anomalies of prenatally diagnosed right aortic arch with concomitant right ductal arch: a systematic review and meta-analysis. *Diagnostics (Basel)*, 2020, 10(10):831. <https://doi.org/10.3390/diagnostics10100831> PMID: 33076538 PMCID: PMC7602867
- [6] Campanale CM, Pasquini L, Santangelo TP, Iorio FS, Bagolan P, Sanders SP, Toscano A. Prenatal echocardiographic assessment of right aortic arch. *Ultrasound Obstet Gynecol*, 2019, 54(1): 96–102. <https://doi.org/10.1002/uog.20098> PMID: 30125417
- [7] Prabhu S, Mehra S, Kasturi S, Tiwari R, Joshi A, John C, Karl TR. Anatomic classification of the right aortic arch. *Cardiol Young*, 2020, 30(11):1694–1701. <https://doi.org/10.1017/S1047951120003601> PMID: 33109287
- [8] D'Antonio F, Khalil A, Zidere V, Carvalho JS. Fetuses with right aortic arch: a multicenter cohort study and meta-analysis. *Ultrasound Obstet Gynecol*, 2016, 47(4):423–432. <https://doi.org/10.1002/uog.15805> PMID: 26643657
- [9] Berg C, Bender F, Soukup M, Geipel A, Axt-Fliedner R, Breuer J, Herberg U, Gembruch U. Right aortic arch detected in fetal life. *Ultrasound Obstet Gynecol*, 2006, 28(7):882–889. <https://doi.org/10.1002/uog.3883> PMID: 17086578
- [10] International Society of Ultrasound in Obstetrics and Gynecology, Carvalho JS, Allan LD, Chaoui R, Copel JA, DeVore GR, Hecher K, Lee W, Munoz H, Paladini D, Tutschek B, Yagel S. ISUOG Practice Guidelines (updated): sonographic screening examination of the fetal heart. *Ultrasound Obstet Gynecol*, 2013, 41(3):348–359. <https://doi.org/10.1002/uog.12403> PMID: 23460196
- [11] Salomon LJ, Alfirevic Z, Berghella V, Bilardo C, Hernandez-Andrade E, Johnsen SL, Kalache K, Leung KY, Malinger G, Munoz H, Prefumo F, Toi A, Lee W; ISUOG Clinical Standards Committee. Practice guidelines for performance of the routine mid-trimester fetal ultrasound scan. *Ultrasound Obstet Gynecol*, 2011, 37(1):116–126. <https://doi.org/10.1002/uog.8831> PMID: 20842655
- [12] Iliescu DG, Comanescu AC, Tudorache S, Cernea N. Right aortic arch with patent right *ductus arteriosus* and normal heart. *Ultrasound Obstet Gynecol*, 2012, 40(1):115–116. <https://doi.org/10.1002/uog.10076> PMID: 21858884
- [13] Bravo C, Gámez F, Pérez R, Álvarez T, De León-Luis J. Fetal aortic arch anomalies: key sonographic views for their differential diagnosis and clinical implications using the cardio-

- vascular system sonographic evaluation protocol. *J Ultrasound Med*, 2016, 35(2):237–251. <https://doi.org/10.7863/ultra.15.02063> PMID: 26715656
- [14] Edwards JE. Vascular rings related to anomalies of the aortic arches. *Mod Concepts Cardiovasc Dis*, 1948, 17(8):1. PMID: 18873268
- [15] Sadler TW. *Langman's medical embryology*. 14th edition, Wolters Kluwer, 2019. <https://meded.lwwhealthlibrary.com/book.aspx?bookid=2487>
- [16] Lodeweges J. Congenital vascular rings. Department of Cardiology, University Medical Centre Groningen, Netherlands, 2020. <https://www.groningencardiology.com/>
- [17] Perolo A, De Robertis V, Cataneo I, Volpe N, Campobasso G, Frusca T, Ghi T, Prandstraller D, Pilu G, Volpe P. Risk of 22q11.2 deletion in fetuses with right aortic arch and without intracardiac anomalies. *Ultrasound Obstet Gynecol*, 2016, 48(2):200–203. <https://doi.org/10.1002/uog.15766> PMID: 26411878
- [18] Maya I, Singer A, Baris HN, Goldberg Y, Shalata A, Khayat M, Ben-Shachar S, Sagi-Dain L. Prenatal microarray analysis in right aortic arch – a retrospective cohort study and review of the literature. *J Perinatol*, 2018, 38(5):468–473. <https://doi.org/10.1038/s41372-018-0062-6> PMID: 29410544
- [19] O'Mahony EF, Hutchinson DP, McGillivray G, Nisbet DL, Palma-Dias R. Right-sided aortic arch in the age of microarray. *Prenat Diagn*, 2017, 37(5):440–445. <https://doi.org/10.1002/pd.5029> PMID: 28207948
- [20] Iliescu D, Tudorache S, Comanescu A, Antsaklis P, Cotarcea S, Novac L, Cernea N, Antsaklis A. Improved detection rate of structural abnormalities in the first trimester using an extended examination protocol. *Ultrasound Obstet Gynecol*, 2013, 42(3):300–309. <https://doi.org/10.1002/uog.12489> PMID: 23595897
- [21] Gheorman L, Iliescu D, Ceaușu I, Paulescu D, Pleșea IE, Gheorman V. Importance of early complex evaluation in high-risk pregnancy associated to diabetes mellitus. Case presentation and review of the literature. *Rom J Morphol Embryol*, 2011, 52(3 Suppl):1127–1132. PMID: 22119836
- [22] Iliescu D, Comănescu A, Antsaklis P, Tudorache Ș, Ghiluișu M, Comănescu V, Paulescu D, Ceaușu I, Antsaklis A, Novac L, Cernea N. Neuroimaging parameters in early open *spina bifida* detection. Further benefit in first trimester screening? *Rom J Morphol Embryol*, 2011, 52(3):809–817. PMID: 21892523
- [23] Dragusin R, Florea M, Iliescu D, Cotarcea S, Tudorache S, Novac L, Cernea N. The contribution and the importance of modern ultrasound techniques in the diagnosis of major structural abnormalities in the first trimester – case reports. *Curr Health Sci J*, 2012, 38(1):20–24. PMID: 24778838 PMID: PMC3945260
- [24] Petrescu AM, Ruican D, Tudorache S, Cernea N, Iliescu D, Marinas M, Genunche-Dumitrescu A, Badea D, Tenea-Cojan TS. Prenatal diagnosis of fetal cardiac abnormalities in the first trimester. *Res Sci Today*, 2020, 20(2):161–168. <https://doi.org/10.38173/RST.2020.20.2.16:161-168>
- [25] Pătru CL, Tudorache Ș, Marinaș MC, Drăgușin RC, Zorilă GL, Nagy RD, Pascu RM, Cernea N. First trimester ultrasound diagnosis of right aortic arch (RAA). *Curr Health Sci J*, 2019, 45(3):296–300. <https://doi.org/10.12865/CHSJ.45.03.08> PMID: 32042458 PMID: PMC6993766
- [26] Șorop-Florea M, Ciurea RN, Ioana M, Stepan AE, Stoica GA, Tănase F, Comănescu MC, Novac MB, Drăgan I, Pătru CL, Drăgușin RC, Zorilă GL, Cărbunaru OM, Oprescu ND, Ceaușu I, Vlădăreanu S, Tudorache Ș, Iliescu DG. The importance of perinatal autopsy. Review of the literature and series of cases. *Rom J Morphol Embryol*, 2017, 58(2):323–337. PMID: 28730216
- [27] Iliescu DG, Cara ML, Tudorache S, Antsaklis P, Novac LV, Antsaklis A, Cernea N. Agenesis of *ductus venosus* in sequential first and second trimester screening. *Prenat Diagn*, 2014, 34(11):1099–1105. <https://doi.org/10.1002/pd.4434> PMID: 24931552
- [28] Iliescu DG, Tudorache S, Cernea D. Agenesis of *ductus venosus* with complex intra- and extrahepatic umbilical drainage. *J Obstet Gynaecol Res*, 2014, 40(4):1163–1164. <https://doi.org/10.1111/jog.12339> PMID: 24698023
- [29] Tudorache S, Cara M, Iliescu DG, Novac L, Cernea N. First trimester two- and four-dimensional cardiac scan: intra- and interobserver agreement, comparison between methods and benefits of color Doppler technique. *Ultrasound Obstet Gynecol*, 2013, 42(6):659–668. <https://doi.org/10.1002/uog.12459> PMID: 23494803
- [30] Evans WN, Acherman RJ, Berthoty D, Mayman GA, Ciccolo ML, Carrillo SA, Restrepo H. Right aortic arch with *situs solitus*. *Congenit Heart Dis*, 2018, 13(4):624–627. <https://doi.org/10.1111/chd.12623> PMID: 30033669
- [31] Velipasaoglu M, Sentürk M, Ayaz R, Atesli B, Tanir HM. Characteristics of prenatally detected right aortic arch cases in a single institution. *J Obstet Gynaecol*, 2018, 38(7):895–898. <https://doi.org/10.1080/01443615.2018.1430126> PMID: 29553860
- [32] Gül A, Güngördük K, Yıldırım G. Perinatal outcomes and anomalies associated with fetal right aortic arch. *J Turk Ger Gynecol Assoc*, 2012, 13(3):184–186. <https://doi.org/10.5152/jtgga.2012.25> PMID: 24592035 PMID: PMC3939238
- [33] Mogra R, Kesby G, Sholler G, Hyett J. Identification and management of fetal isolated right-sided aortic arch in an unselected population. *Ultrasound Obstet Gynecol*, 2016, 48(6):739–743. <https://doi.org/10.1002/uog.15892> PMID: 26918379
- [34] Razon Y, Berant M, Fogelman R, Amir G, Birk E. Prenatal diagnosis and outcome of right aortic arch without significant intracardiac anomaly. *J Am Soc Echocardiogr*, 2014, 27(12):1352–1358. <https://doi.org/10.1016/j.echo.2014.08.003> PMID: 25240492
- [35] Wójtowicz A, Respondek-Liberska M, Słodki M, Kordjalik P, Plużańska J, Knafel A, Huras H. The significance of a prenatal diagnosis of right aortic arch. *Prenat Diagn*, 2017, 37(4):365–374. <https://doi.org/10.1002/pd.5020> PMID: 28177551
- [36] Yerlikaya G, Efe Türk T, Springer S, Reischer T. Prenatal detection of right aortic arch. *Arch Gynecol Obstet*, 2019, 299(4):933–938. <https://doi.org/10.1007/s00404-019-05056-5> PMID: 30706183 PMID: PMC6435603
- [37] Oztunc F, Ugan Atik S, Dedeoglu R, Yuksel MA, Madazlı R. Aortic arch anomalies detected in foetal life by echocardiography. *J Obstet Gynaecol*, 2018, 38(5):647–651. <https://doi.org/10.1080/01443615.2017.1399989> PMID: 29430994
- [38] Bronshtein M, Zimmer EZ, Blazer S, Blumenfeld Z. Right *ductus arteriosus*: facts and theory. *Eur J Obstet Gynecol Reprod Biol*, 2011, 159(2):282–288. <https://doi.org/10.1016/j.ejogrb.2011.07.047> PMID: 21925785
- [39] Yoo SJ, Min JY, Lee YH, Roman K, Jaeggi E, Smallhorn J. Fetal sonographic diagnosis of aortic arch anomalies. *Ultrasound Obstet Gynecol*, 2003, 22(5):535–546. <https://doi.org/10.1002/uog.897> PMID: 14618670
- [40] Valletta EA, Pregarz M, Bergamo-Andreis IA, Boner AL. Tracheoesophageal compression due to congenital vascular anomalies (vascular rings). *Pediatr Pulmonol*, 1997, 24(2):93–105. [https://doi.org/10.1002/\(sici\)1099-0496\(199708\)24:2<93::aid-ppul4>3.0.co;2-j](https://doi.org/10.1002/(sici)1099-0496(199708)24:2<93::aid-ppul4>3.0.co;2-j) PMID: 9292900
- [41] Miranda JO, Callaghan N, Miller O, Simpson J, Sharland G. Right aortic arch diagnosed antenatally: associations and outcome in 98 fetuses. *Heart*, 2014, 100(1):54–59. <https://doi.org/10.1136/heartjnl-2013-304860> PMID: 24192976
- [42] Wood JA, Carachi R. The right-sided aortic arch in children with oesophageal atresia and tracheo-oesophageal fistula. *Eur J Pediatr Surg*, 2012, 22(1):3–7. <https://doi.org/10.1055/s-0031-1285906> PMID: 21960429
- [43] Shah RK, Mora BN, Bacha E, Sena LM, Buonomo C, Del Nido P, Rahbar R. The presentation and management of vascular rings: an otolaryngology perspective. *Int J Pediatr Otorhinolaryngol*, 2007, 71(1):57–62. <https://doi.org/10.1016/j.ijporl.2006.08.025> PMID: 17034866
- [44] Guo Q, Kong Y, Zeng S, Zhou J, Wang X, Shang Q, Zhou J, Yuan H, Wang L, Tong L, Yi A, Zhou Q. Fetal double aortic arch: prenatal sonographic and postnatal computed tomography angiography features, associated abnormalities and clinical outcomes. *BMC Pregnancy Childbirth*, 2020, 20(1):614. <https://doi.org/10.1186/s12884-020-03300-4> PMID: 33046002 PMID: PMC7552480
- [45] Strife JL, Bisset GS III, Burrows PE. Cardiovascular system. In: Kirks DR, Griscom NT (eds). *Practical pediatric radiology: diagnostic radiology of infants and children*. 3rd edition, Lippincott-Raven, Philadelphia, 1998.
- [46] Cinà CS, Arena GO, Bruin G, Clase CM. Kommerell's diverticulum and aneurysmal right-sided aortic arch: a case report and review of the literature. *J Vasc Surg*, 2000,

- 32(6):1208–1214. <https://doi.org/10.1067/mva.2000.108012> PMID: 11107094
- [47] Felson B, Palayew MJ. The two types of right aortic arch. *Radiology*, 1963, 81(5):745–759. <https://doi.org/10.1148/81.5.745> PMID: 14073842
- [48] Zidere V, Tsapakis EG, Huggon IC, Allan LD. Right aortic arch in the fetus. *Ultrasound Obstet Gynecol*, 2006, 28(7): 876–881. <https://doi.org/10.1002/uog.3841> PMID: 17066500
- [49] Momma K, Matsuoka R, Takao A. Aortic arch anomalies associated with chromosome 22q11 deletion (CATCH 22). *Pediatr Cardiol*, 1999, 20(2):97–102. <https://doi.org/10.1007/s002469900414> PMID: 9986884
- [50] Luo Q, Chen J, Zhang Y, Li J, Su X, Wang Q, Ding Y. Incidence of chromosomal anomalies in fetuses with isolated right aortic arch: a meta-analysis. *Prenat Diagn*, 2020, 40(3): 294–300. <https://doi.org/10.1002/pd.5606> PMID: 31736147
- [51] Trairisilp K, Tongprasert F, Srisupundit K, Luewan S, Tongsong T. Prenatal screening of DiGeorge (22q11.2 deletion) syndrome by abnormalities of the great arteries among Thai pregnant women. *Obstet Gynecol Sci*, 2020, 63(3):330–336. <https://doi.org/10.5468/ogs.2020.63.3.330> PMID: 32489978 PMID: PMC7231935
- [52] Wu X, Li Y, Su L, Xie X, Cai M, Lin N, Huang H, Lin Y, Xu L. Chromosomal microarray analysis for the fetuses with aortic arch abnormalities and normal karyotype. *Mol Diagn Ther*, 2020, 24(5):611–619. <https://doi.org/10.1007/s40291-020-00474-7> PMID: 32651932 PMID: PMC7497298

Corresponding authors

Ciprian Laurențiu Pătru, MD, PhD, Department of Mother and Child, University of Medicine and Pharmacy of Craiova, 2 Petru Rareș Street, 200349 Craiova, Dolj County, Romania; Phone +40761–632 298, e-mail: patru_ciprian@yahoo.com

Anca-Maria Istrate-Ofițeru, MD, PhD, Department of Histology, University of Medicine and Pharmacy of Craiova, 2 Petru Rareș Street, 200349 Craiova, Dolj County, Romania; Phone +40764–836 619, e-mail: ancaofiteru92@yahoo.com

Received: January 23, 2021

Accepted: May 27, 2021